## REMARKS

Claims 1, 5-13, 16-18 and 38-50 remain in the application for further prosecution. Claims 1 and 38 have been amended to distinguish the Shartle reference.

### Rejection Under 35 U.S.C. 112

Claims 1, 5-13, 16-18 and 38-50 have been rejected under 35 U.S.C. 112, second paragraph as being incomplete. In the above amendment the Examiner's suggested revision has been adopted, thus obviating the rejections. The phrase "between two vents" has been added to further define the position of the transfer capillary passageway, which position distinguishes the Shartle reference.

### Rejection Under 35 U.S.C. 102

Claims 1 and 38 have been rejected under 35 U.S.C. 102 (b) as anticipated by Shartle, et al. ("Shartle"), U.S. 5,230,866. The '866 patent teaches improved "stop-flow junctions", which are defined by Shartle as places where liquid flowing by capillary action stops until some outside force is applied. In some aspects, the capillary stops of the present applicants could be considered to be stop-flow junctions. However, the improvements disclosed by Shartle are unique. In particular, Shartle proposed blocking an external vent to build air pressure that assists in stopping liquid flowing in a capillary at a stop-flow junction. He also proposed using a nozzle designed to assist stopping liquid flow at the entrance to a chamber and using a rupture junction to relieve pressure creating by closing of valves in his device.

The Examiner has cited passages in Shartle to support his rejection for anticipation. These will be considered in more detail below. However, it should be understood that the Shartle disclosure in principally directed to a device which is referred to as a "diluter". A measured liquid sample is moved by releasing diluents to push the sample from one end of a measuring passageway and out the opposite end into a mixing chamber. In the following comparison of Claim 1 with Shartle, his Fig 5 will be emphasized in response to the Examiners comments. Fig. 5 is described at column 13, lines 14-57. In the diluter, the sample is not transferred from <u>between</u> two vents to a chamber, but instead it is transferred from one end of a capillary into the chamber, followed by the diluent with which it is than mixed.

| **Amended Claim 1** | **Shartle** |
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| 1. A device for dispersing and analyzing a | • Shartle is principally concerned with improved "stop-flow junctions", but he does |

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| uniform volume of a liquid sample comprising: | describe an example is which a uniform volume of a sample is analyzed. |
| (a) a sample well for receiving a portion of said liquid sample; | • Shartle shows a sample inlet (110) but it can be merely an opening and it is not a sample well as shown by the Applicants. The cited description at column 14, line 64 to column 15, line 15 does not describe a sample well as defined by the present invention. |
| (b) a hydrophilic capillary passageway communicating with said sample well of (a) for receiving said liquid from said sample well by capillary action, said passageway including a segment defining said uniform volume of said liquid sample, | • Shartle does provide a capillary passageway (120) from his sample inlet (110) which enters an inverted T-shaped passage terminated at stops (146) (145) and (147). (146) appears to be vented to atmosphere, but (147) is a closed rupture junction and (145) is <u>not</u> vented because (104) is <u>closed</u> to assist (145). Stop 145 is a "vent-assisted" stop flow junction (see column 8, line 56 et seq.) Thus, the sample is <u>not</u> defined between two vents to the atmosphere, only <u>one</u> vent to atmosphere is used. |
| said uniform volume being disposed between two vents from said passageway to the atmosphere, | • In Fig. 5, it is not clear that the segment is defined, since valve (202) is used to rupture junction 147, which said to dispose of excess sample into 148 (Shown as 140 in Fig. 5). The segment appears to be 140a and 140b, (see column 13, lines 18-19)which is <u>not</u> defined as being between two vents to atmosphere.. |
| said segment in liquid communication between said two vents with a transfer hydrophilic capillary passageway for transferring said uniform volume of said liquid sample from the segment defining said uniform volume of said liquid sample being between two vents to a first reagent well; and | • Shartle's device does not provide a transfer capillary from his measuring chamber (140a and 140b). In Fig. 5 the measuring chamber 140b terminates at mixing chamber 150 and diluent from 175 is used to push the sample from 140 into 150 by overcoming stop 145. Since the measuring chamber (140a and 140b) terminates at mixing chamber (150) <u>no transfer capillary is present</u>. Furthermore, the transfer passageway is now defined as connecting the measuring segment from <u>between</u> the vents to atmosphere to a first reagent cell. The passage at column 17, line 62 |

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| | to column 18, line 2 describes a passageway through which diluent flows into the measuring chamber (140a and 140b) to expel the sample and diluent into the mixing chamber. |
| (c) a hydrophilic capillary stop disposed within said transfer hydrophilic capillary passageway for preventing transfer of said uniform sample volume until the resistance of said stop is overcome by a mean for applying force other than centrifugal force. | • Shartle has no transfer passageway and thus could have no capillary stop in the passageway. In the present invention, the stop is overcome in order to empty the segment between the vents to atmosphere. In Shartle the sample is displaced by diluent and the measuring chamber is not emptied from between vents to atmosphere. |

The above comparison applies also to independent claim 38.

The Examiner has responded to the Applicant's previous arguments related to Shartle. He has stated that "capillary passageway 120 and uniform volume segment 140a are located between the vent 1 (110) and a second vent 104 that vents to the atmosphere." As discussed above, 104 is <u>not</u> a vent unless 105 is open. However, as Shartle makes clear at column 8, lines 56 et seq. 105 is closed when a sample is introduced so that the liquid stops at 145, the entrance to the mixing chamber 150. Furthermore, after the valve 202 opens rupture junction 147 the excess liquid flows into 148 (140 in Fig. 5) (see column 13, lines 34-44). Therefore, the measured volume (140a and 140b) appears to be open to atmosphere at 110 and 146, but <u>not</u> at 145 and thus is not defined as <u>between</u> the two vents to atmosphere.

The Examiner now defines as a transfer capillary from the measuring Chamber (140a and 140b) the capillary between 147 and the intersection of 120 and 140a. That capillary section is emptied into 140 after 147 is ruptured, (see column 13, lines 34-44). Therefore it is <u>not</u> a transfer capillary <u>from</u> the measuring chamber to a first reagent well. 140 (actually 148) is a waste chamber. The mixing chamber 150 actually receives the sample directly from the measuring chamber 140a and 140b when diluent is released from 175. Thus, there is <u>no</u> transfer capillary extending from the measuring chamber 140a and 140b to the mixing chamber 150.

In his interpretation of Fig. 5, the Examiner mistakes 140 (sic148) to receive the measured sample, but actually it receives <u>excess</u> sample. The measured volume is pushed into 150 by diluent.

The Applicants submit that in view of the differences discussed above, that Shartle does not anticipate the amended claims.

**Rejection under 35 U.S.C. 103**

Claims 1, 5-13, 16-18, and 38-50 have been rejected under 35 U.S.C. 103(a) as unpatentable (i.e. obvious) over McNeely, et al. (US 6,296,020)("McNeely '020") in view of Kellogg, et al. (US 6,063,589("Kellogg") and further in view of McNeely, et al. (US 6,615,856)("McNeely '856").

The Examiner has repeated his previous rejections based on McNeely '020, Kellogg and McNeely '856. McNeely '020 does not show a sample well, which supplies a reagent well with a sample volume defined by a segment of a hydrophilic capillary which is disposed between two vents. Instead, McNeely '020 has been cited for its teaching of physical principles, rather than for a device related to the Applicant's microfluidic device. Therefore, McNeely '020 is not a typical principal reference under 35 U.S.C. 103, which contains omissions to be supplied by the secondary reference.

In general, McNeely '020 shows devices for splitting liquid into multiple wells or combining several liquids in a single well, using passive stops. McNeely '020 evidently preferred using hydrophobic passageways with aqueous liquids, combined with hydrophilic stops (see column 3, lines 59-62, the discussion above and the claims). McNeely '020 does not show a sample well connected to a capillary passageway that contains a segment defining a sample volume, which is transferred to a reagent well. The Examiner's citations of the McNeely '020 patent were discussed in a table in a previous amendment. That table is repeated and expanded below.

| Examiner | McNeely |
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| o "plurality of sample well" (figs. 3a-d) | o Example 2 discusses Figs. 3a – d. No sample well is shown. Instead liquid is split into four wells using a series of four stops to assist division of the liquid. The liquid is defined by the volume of the wells, not by a segment of a capillary passageway. |

| Examiner | McNeely |
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| o “hydrophilic capillary....in fluid communication with a sample well” (col. 5, lines 39-41) | o This citation merely makes a general statement about hydrophilic materials. No hydrophilic capillary communicating with a sample well is shown. |
| o “segment defining a volume....disposed between two vents” (col. 4, lines 8-10; col. 4, lines 50-55; Fig. E-G; col. 9, lines 13-60; col. 11, lines 1-16) | o Col. 4, lines 8-10 describes no segment defining a volume between two vents.<br><br>Col. 4, lines 50-55 describes an air vent where two liquid capillaries join. Described also at column 9, lines 19-60. No segment is defined as part of a capillary between two vents.<br>”Figs. E-G” may refer to fig. 3E-G. If so, these figures relate to filling parallel wells that are <u>not</u> defined between two vents.<br>Col. 11, lines 1-16 describes the use of gas to push liquid past the stops, not to define a fixed volume in a capillary passageway. |
| o “hydrophilic capillary stop disposed within the hydrophilic passageway for preventing sample transport” (col. 5, lines 50-59; col. 6, lines 11-47; col. 8, lines 64-68; col. 9, lines 3-14) | o Col. 5, lines 50-59 merely describes the function of a capillary stop.<br>Col. 6, lines 11-47 continues the general description of the pressure barriers, i.e., capillary stops.<br>Col. 8, lines 64-68 further illustrates hydrophilic and hydrophobic stops.<br>Col. 9, lines 3-14 does not describe capillary stops, but division of a sample into multiple wells. |
| o “demonstrate capillary action (col. 5, lines 30-49)...0.1 to 1000 micron...inherently have capillary action when liquid is present”. | o Col 5, lines 30-49 merely provides a general discussion of capillarity and then discusses “pressure barriers” in lines 50-59. The Applicants use capillary and pressure barriers (stops) but it is their mode of use that is claimed, <u>not</u> the underlying physical principles. |

| Examiner | McNeely |
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| o "As seen in figures 8a-8c...stopping means exist at the right of each of the 4 initial wells...Air or gas is pushed through the ports...will displace the fluid downstream past the stopping means...air escape ducts...allow displaced air to exit so fluid can fill the consolidation well". | o Fig. 8 A-C are discussed at col. 11, lines 1-16. Air is forced into the 4 initial wells to displace liquid into a consolidation well. This method is of no more than general interest with respect to the Applicant's invention as now claimed, because liquid in a defined capillary segment is not transferred from between air vents by a transfer capillary. |

From this table, it should be clear that McNeely '020 fails to support the Examiner's position. McNeely '020 does not just lack the use of a hydrophilic capillary to transfer liquid, but he fails to describe a device that separates from a larger sample a defined volume in a capillary segment and transfers that defined volume to a reagent well. McNeely '020 appears to teach that use of a second liquid or a gas to force a first liquid past capillary stops. Also, since he appears to use hydrophobic passageways with water-based liquids, it is implied that capillary forces are not used to transport liquid.

Kellogg describes devices in which centrifugal force is used to transfer liquids after a sample liquid fills the group of capillaries used to define the sample volume to be tested. The Applicant's claims exclude the use of centrifugal force. The sample volume is not defined by a portion of a hydrophilic capillary positioned between two vents, but instead an array of capillaries is defined as between a chamber at one end and the sample well at the other end (the excess sample having been sent using centrifugal force to the over flow well). Thus, Kellogg does not teach the use of a capillary segment that connects to a transfer capillary between two vents.

McNeely '020 does not show essential elements of the Applicants' claimed invention and forces liquid through with other liquids or gas. Kellogg relies on increasing centrifugal force to transfer liquid through his devices. There is no reason why one skilled in the art would consider a combination of McNeely '020 and Kellogg. The Kellogg devices are designed to move liquid and expel air with increasing centrifugal force and therefore are not combinable with the McNeely '020 devices. Kellogg would have to redesign his device to be operated by a driving liquid or gas as done by McNeely. Alternatively, McNeely '020 would have to be redesigned to

operate by centrifugal force. Consequently, different devices would be provided, but not those of McNeely '020 or of Kellogg, since they have different objectives.

The McNeely '856 patent teaches a method of controlling fluid flow in a microfluidic device in which external valves and pumps are employed (see Abstract). Since capillary forces are not used by McNeely's devices, the flow of liquids is controlled by opening and closing vents. As he shows in Fig. 1 A-C, liquid flow is stopped beyond an air vent since the external force applied is not able to compress the air trapped in the dead-ended passageway. The general approach is discussed in the section entitled "Flow Barriers" (column 4, line 33 et seq.). As McNeely observes "if capillary forces cannot be relied upon, ...then alternative methods of fluid control are needed" (column 4, lines 37-40). "An alternative to capillary stop junctions and the like are pneumatic pressure barriers" (column 4, lines 45-46). It appears then, that McNeely '856 is not pertinent to the Applicant's invention.

Consequently, the Examiner is asked to enter the proposed amendments and then to reconsider his rejection and allow the claims as amended. If further amendment is believed necessary, the Examiner is invited to contact the Applicants' attorney at the telephone number provided below.

Respectfully submitted,

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Date

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